

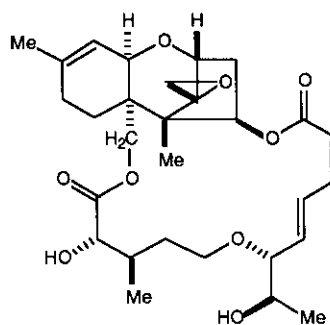
A STEREoselective SYNTHESIS OF (2Z,4E)-DIENOIC ACID INVOLVING
MASKED FUNCTIONAL GROUPS: $n\text{-Bu}_4\text{NF}$ INDUCED RING-OPENING OF
 α,β -UNSATURATED δ -LACTONE

Tadashi Nakata,* Noriaki Hata, and Takeshi Oishi*

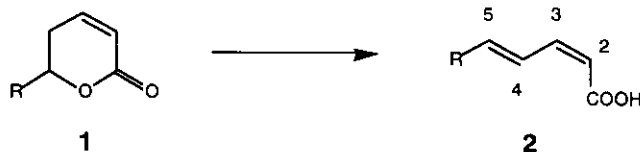
RIKEN (The Institute of Physical and Chemical Research), Wako-shi,
Saitama 351-01, Japan

Abstract — $n\text{-Bu}_4\text{NF}$ induced ring-opening of α,β -unsaturated δ -lactone produced (2Z,4E)-dienoic acid without affecting acetoxyl groups present in the side chain of the lactone ring.

(2Z,4E)-Dienoic acid moieties are often found in biologically active natural products such as rifamycins, macbecins, and roridins.¹⁾ A base-induced ring opening of α,β -unsaturated δ -lactones **1** is considered to be one of the most reliable methods for the synthesis of (2Z,4E)-dienoic acids **2**, in which strong bases such as MeONa, $t\text{-BuOK}$, and MeSNa have been used.²⁾ In the course of searching much milder conditions which can be applied for lactones involving other functional groups, we found that $n\text{-Bu}_4\text{NF}$ was an extremely



Roridin A

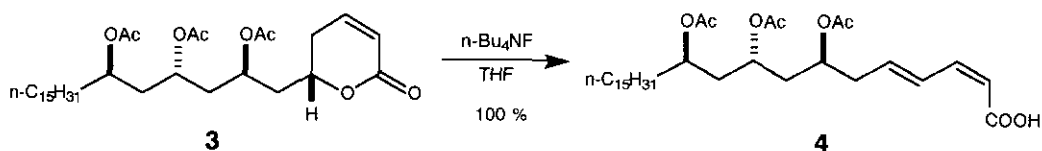


a: R = PhCH_2CH_2 , **b:** R = $t\text{-Bu}$

effective reagent for this purpose.^{cf.3)} Namely, by using 3~5 molar equiv. of $n\text{-Bu}_4\text{NF}$ as a base, the α,β -unsaturated δ -lactones **1a** and **1b** were converted to **2a** and **2b**, respectively, with virtually quantitative yields.

A typical procedure is as follows: A mixture of lactone **1a** (20 mg; 99 μ mol) and $n\text{-Bu}_4\text{NF}\cdot 3\text{H}_2\text{O}$ (156 mg; 0.49 mmol) in THF (2 ml) was stirred at room temperature for 30 min under argon. Water was added and the mixture was extracted with ethyl acetate. The organic layer was washed with 10% HCl, sat. NaCl solution, and dried over MgSO_4 . The solvent was evaporated in vacuo and the residue was purified on silica gel column chromatography (AcOEt : n -hexane = 1 : 3) to give dienoic acid **2a** (19.6 mg; 98% yield). The stereochemistry of the product **2a** was confirmed based on ^1H -nmr data; δ 5.60 (2-H), 6.13 (5-H), 6.63 (3-H), 7.39 (4-H); $J_{2,3}=11.0$ Hz, $J_{3,4}=11.0$ Hz, $J_{4,5}=15.3$ Hz.

The present reaction could be applied to the substrate **3** possessing a long side-chain involving three acetoxyl groups. It should be emphasized here that the three acetoxyl groups in **3** were remained completely unaffected in the product **4** after ring opening. The previously used strong bases are presumed to cause



hydrolysis of the acetates present in the side chain.²⁾ The present reaction with this particular feature constitutes one of the crucial chemical steps in our new strategy for determining the stereostructure of 1,3-polyols involved in polyene macrolide antibiotics.⁴⁾

REFERENCES

- 1) B.B.Jarvis and E.P.Mazzola, *Acc. Chem. Res.*, 1982, **15**, 388.
- 2) a) U. Eisner, J. A. Elvidge, and R. P. Linstead, *J. Chem. Soc.*, 1953, 1372; b) G. Cardillo, M. Orena, and S. Sandri, *Tetrahedron*, 1976, **32**, 107; c) E. J. Corey and G. Schmidt, *Tetrahedron Lett.*, 1979, 2317; d) W. R. Roush and A. P. Spada, *Tetrahedron Lett.*, 1982, **23**, 3773; e) S. Masamune, B. Imperiali, and D. S. Garvey, *J. Am. Chem. Soc.*, 1982, **104**, 5528.
- 3) See reference 5 in the following paper: T. Nakata, N. Hata, K. Iida, and T. Oishi, *Tetrahedron Lett.*, 1987, **28**, 5661.
- 4) T. Nakata, N. Hata, T. Suenaga, and T. Oishi, presented at the 30th Symposium on the Chemistry of Natural Products at Fukuoka, October, 1988. Symposium papers, p. 540.

Received, 30th August, 1989